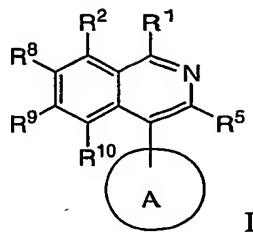


WHAT IS CLAIMED IS:

1. A compound of formula I



5

or a pharmaceutically acceptable salt, crystal form, or hydrate, wherein:

A is

a) an aryl ring, wherein any stable aryl ring atom is independently unsubstituted or substituted with

- 1) halogen,
- 2) NO₂,
- 3) CN,
- 4) CR⁴⁶=C(R⁴⁷R⁴⁸)₂,
- 5) C≡C R⁴⁶,
- 6) (CRⁱR^j)_rOR⁴⁶,
- 7) (CRⁱR^j)_rN(R⁴⁶R⁴⁷),
- 8) (CRⁱR^j)_rC(O)R⁴⁶,
- 9) (CRⁱR^j)_rC(O)OR⁴⁶,
- 10) (CRⁱR^j)_rR⁴⁶,
- 11) (CRⁱR^j)_rS(O)O-₂R⁶¹,
- 12) (CRⁱR^j)_rS(O)O-₂N(R⁴⁶R⁴⁷),
- 13) OS(O)O-₂R⁶¹,
- 14) N(R⁴⁶)C(O)R⁴⁷,
- 15) N(R⁴⁶)S(O)O-₂R⁶¹,
- 16) (CRⁱR^j)_rN(R⁴⁶)R⁶¹,
- 17) (CRⁱR^j)_rN(R⁴⁶)R⁶¹OR⁴⁷,
- 18) (CRⁱR^j)_rN(R⁴⁶)(CR^kR^l)_sC(O)N(R⁴⁷R⁴⁸),
- 19) N(R⁴⁶)(CRⁱR^j)_rR⁶¹,
- 20) N(R⁴⁶)(CRⁱR^j)_rN(R⁴⁷R⁴⁸),
- 21) (CRⁱR^j)_rC(O)N(R⁴⁷R⁴⁸),

22) oxo,

b) a heteroaryl ring selected from the group consisting of

a 5-membered unsaturated monocyclic ring with 1, 2, 3 or 4 heteroatom ring atoms selected from the group consisting of N, O or S,

5 a 6-membered unsaturated monocyclic ring with 1, 2, 3 or 4 heteroatom ring atoms selected from the group consisting N, O and S, and

a 9- or 10-membered unsaturated bicyclic ring with 1, 2, 3 or 4 heteroatom ring atoms selected from the group consisting of N, O or S,

10 wherein any stable S heteroaryl ring atom is unsubstituted or mono- or di-substituted with oxo, and any stable C or N heteroaryl ring atom is independently unsubstituted or substituted with

1) halogen,

2) NO₂,

3) CN,

4) CR⁴⁶=C(R⁴⁷R⁴⁸)₂,

5) C≡C R⁴⁶,

6) (CRⁱR^j)_rOR⁴⁶,

7) (CRⁱR^j)_rN(R⁴⁶R⁴⁷),

8) (CRⁱR^j)_rC(O)R⁴⁶,

9) (CRⁱR^j)_rC(O)OR⁴⁶,

10) (CRⁱR^j)_rR⁴⁶,

11) (CRⁱR^j)_rS(O)O-2R⁶¹,

12) (CRⁱR^j)_rS(O)O-2N(R⁴⁶R⁴⁷),

13) OS(O)O-2R⁶¹,

14) N(R⁴⁶)C(O)R⁴⁷,

15) N(R⁴⁶)S(O)_xR⁶¹,

16) (CRⁱR^j)_rN(R⁴⁶)R⁶¹,

17) (CRⁱR^j)_rN(R⁴⁶)R⁶¹OR⁴⁷,

18) (CRⁱR^j)_rN(R⁴⁶)(CR^kR^l)_sC(O)N(R⁴⁷R⁴⁸),

19) N(R⁴⁶)(CRⁱR^j)_rR⁶¹,

20) N(R⁴⁶)(CRⁱR^j)_rN(R⁴⁷R⁴⁸),

21) (CRⁱR^j)_rC(O)N(R⁴⁷R⁴⁸), or

22) oxo, or

c) a 4-, 5- or 6-membered heterocyclic ring containing 1 or 2 nitrogen atoms, unsubstituted, mono-substituted or di-substituted with C₁-C₆ alkyl;

Y is CH_2 , NR^{53} , NC(O)R^{53} , S(O)O-2 or O ;

G is H_2 or O ;

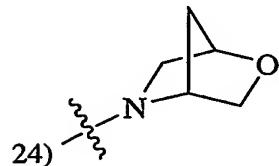
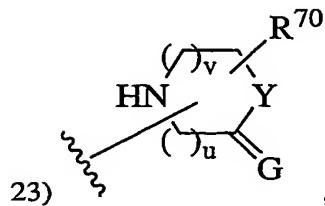
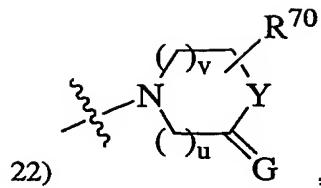
R^a , R^b , R^c , R^d , R^e , R^f , R^g , R^h , R^i , R^j , R^k , and R^l are independently selected from the group consisting of:

- 5 1) hydrogen,
- 2) $\text{C}_1\text{-C}_6$ alkyl,
- 3) halogen,
- 4) aryl,
- 5) R^{80} ,
- 10 6) $\text{C}_3\text{-C}_{10}$ cycloalkyl, and
- 7) OR^4 ,

said alkyl, aryl, and cycloalkyl being unsubstituted, monosubstituted with R^7 , disubstituted with R^7 and R^{15} , trisubstituted with R^7 , R^{15} and R^{16} , or tetrasubstituted with R^7 , R^{15} , R^{16} and R^{17} ;

R^1 is independently selected from:

- 15 1) hydrogen,
- 2) halogen,
- 3) NO_2 ,
- 4) CN ,
- 5) $\text{CR}^{40}=\text{C}(\text{R}^{41}\text{R}^{42})$,
- 20 6) $\text{C}\equiv\text{CR}^{40}$,
- 7) $(\text{CR}^a\text{R}^b)_n\text{OR}^{40}$,
- 8) $(\text{CR}^a\text{R}^b)_n\text{N}(\text{R}^{40}\text{R}^{41})$,
- 9) $(\text{CR}^a\text{R}^b)_n\text{C(O)R}^{40}$,
- 10) $(\text{CR}^a\text{R}^b)_n\text{C(O)OR}^{40}$,
- 25 11) $(\text{CR}^a\text{R}^b)_n\text{R}^{40}$,
- 12) $(\text{CR}^a\text{R}^b)_n\text{S(O)O-2R}^6$,
- 13) $(\text{CR}^a\text{R}^b)_n\text{S(O)O-2N(R}^{40}\text{R}^{41})$,
- 14) OS(O)O-2R^6 ,
- 15) $\text{N(R}^{40})\text{C(O)R}^{41}$,
- 30 16) $\text{N(R}^{40})\text{S(O)O-2R}^6$,
- 17) $(\text{CR}^a\text{R}^b)_n\text{N(R}^{40})\text{R}^6$,
- 18) $(\text{CR}^a\text{R}^b)_n\text{N(R}^{40})\text{R}^6\text{OR}^{41}$,
- 19) $(\text{CR}^a\text{R}^b)_n\text{N(R}^{40})(\text{CR}^c\text{R}^d)_t\text{C(O)N(R}^{41}\text{R}^{42})$,
- 20) $\text{N(R}^{40})(\text{CR}^a\text{R}^b)_n\text{R}^6$,
- 35 21) $\text{N(R}^{40})(\text{CR}^a\text{R}^b)_n\text{N(R}^{41}\text{R}^{42})$,



25) $(CR^aR^b)_nC(O)N(R^{41}R^{42})$, and

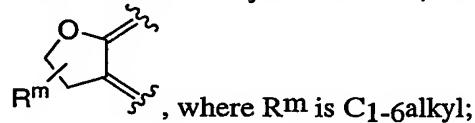
5 26) a 4-, 5-, or 6-membered heterocyclic ring containing 1 nitrogen atom, unsubstituted, or mono-, di- or tri-substituted with -OH;

R^2 , R^8 , R^9 and R^{10} are independently selected from:

- 1) hydrogen,
- 2) halogen,
- 10 3) NO_2 ,
- 4) CN ,
- 5) $CR^{43}=C(R^{44}R^{45})$,
- 6) $C\equiv CR^{43}$,
- 7) $(CRERF)_pOR^{43}$,
- 15 8) $(CRERF)_pN(R^{43}R^{44})$,
- 9) $(CRERF)_pC(O)R^{43}$,
- 10) $(CRERF)_pC(O)OR^{43}$,
- 11) $(CRERF)_pR^{43}$,
- 12) $(CRERF)_pS(O)_{0-2}R^{60}$,
- 20 13) $(CRERF)_pS(O)_{0-2}N(R^{43}R^{44})$,
- 14) $OS(O)_{0-2}R^{60}$,
- 15) $N(R^{43})C(O)R^{44}$,

16) $N(R^{43})S(O)_{0-2}R^{60}$,
 17) $(CReRF)_pN(R^{43})R^{60}$,
 18) $(CReRF)_pN(R^{43})R^{60}OR^{44}$,
 19) $(CReRF)_pN(R^{43})(CRgRh)_qC(O)N(R^{44}R^{45})$,
 20) $N(R^{43})(CReRF)_pR^{60}$,
 21) $N(R^{43})(CReRF)_pN(R^{44}R^{45})$, and
 22) $(CReRF)_pC(O)N(R^{43}R^{44})$,

5 or R^2 and R^8 are independently as defined above, and R^9 and R^{10} , together with the atoms to which they are attached, form the ring



R^4 , R^{40} , R^{41} , R^{42} , R^{43} , R^{44} , R^{45} , R^{46} , R^{47} , R^{48} , R^{49} , R^{50} , R^{51} , R^{52} , and R^{53} are independently selected from:

15 1) hydrogen,
 2) C₁-C₆ alkyl,
 3) C₃-C₁₀ cycloalkyl,
 4) aryl,
 5) R^{81} ,
 6) CF₃,
 7) C₂-C₆ alkenyl, and
 20 8) C₂-C₆ alkynyl,

25 said alkyl, aryl, and cycloalkyl is unsubstituted, mono-substituted with R^{18} , di-substituted with R^{18} and R^{19} , tri-substituted with R^{18} , R^{19} and R^{20} , or tetra-substituted with R^{18} , R^{19} , R^{20} and R^{21} ;
 R^5 is independently selected from:

30 1) hydrogen,
 2) halogen,
 3) CN,
 4) $C(O)N(R^{49}R^{50})$,
 5) $C(O)OR^{49}$,
 6) $S(O)_{0-2}N(R^{49}R^{50})$,
 7) $S(O)_{0-2}R^{62}$,
 8) C₁-C₆ alkyl,
 9) C₃-C₁₀ cycloalkyl,
 10) R^{82} ,

said alkyl, aryl, and cycloalkyl is unsubstituted, mono-substituted with R²², di-substituted with R²² and R²³, tri-substituted with R²², R²³ and R²⁴, or tetra-substituted with R²², R²³, R²⁴ and R²⁵;
R⁶, R⁶⁰, R⁶¹, R⁶² and R⁶³ are independently selected from:

- 1) C₁-C₆ alkyl,
- 2) aryl,
- 3) R⁸³, and
- 4) C₃-C₁₀ cycloalkyl;

said alkyl, aryl, and cycloalkyl is unsubstituted, mono-substituted with R²⁶, di-substituted with R²⁶ and R²⁷, tri-substituted with R²⁶, R²⁷ and R²⁸, or tetra-substituted with R²⁶, R²⁷, R²⁸ and R²⁹;

R⁷, R¹⁵, R¹⁶, R¹⁷, R¹⁸, R¹⁹, R²⁰, R²¹, R²², R²³, R²⁴, R²⁵, R²⁶, R²⁷, R²⁸, R²⁹, and R⁷⁰ are independently selected from:

- 1) C₁-C₆ alkyl,
- 2) halogen,
- 3) OR⁵¹,
- 4) CF₃,
- 5) aryl,
- 6) C₃-C₁₀ cycloalkyl,
- 7) R⁸⁴,
- 8) S(O)₀₋₂N(R⁵¹R⁵²),
- 9) C(O)OR⁵¹,
- 10) C(O)R⁵¹,
- 11) CN,
- 12) C(O)N(R⁵¹R⁵²),
- 13) N(R⁵¹)C(O)R⁵²,
- 14) S(O)₀₋₂R⁶³,
- 15) NO₂, and
- 16) N(R⁵¹R⁵²);

R⁸⁰, R⁸¹, R⁸², R⁸³ and R⁸⁴ are independently selected from a group of unsubstituted or substituted

30 heterocyclic rings consisting of a 4-6 membered unsaturated or saturated monocyclic ring with 1, 2, 3 or 4 heteroatom ring atoms selected from the group consisting N, O and S, and a 9- or 10-membered unsaturated or saturated bicyclic ring with 1, 2, 3 or 4 heteroatom ring atoms selected from the group consisting of N, O or S;

n, p, q, r, s and t are independently 0, 1, 2, 3, 4, 5 or 6;

u is 0, 1 or 2; and

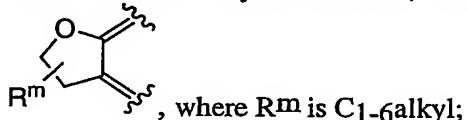
v is 0, 1 or 2.

2. A compound of Claim 1, or a pharmaceutically acceptable salt thereof, wherein:

5 A is a) an aryl ring selected from phenyl, unsubstituted or substituted as in Claim 1, b) a heteroaryl ring, unsubstituted or substituted as in Claim 1, selected from the group consisting of pyridine, pyrimidine, pyrazine, pyridazine, indole, pyrrolopyridine, benzimidazole, benzoxazole, benzothiazole, and benzoxadiazole, or c) a 4-, 5- or 6-membered heterocyclic ring as defined in Claim 1;
R², R⁸, R⁹ and R¹⁰ are independently selected from the group consisting of:

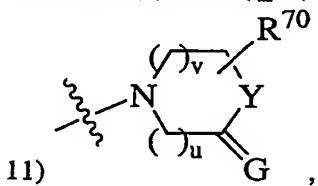
10 1) hydrogen,
2) halogen,
3) OR⁴³, and
4) (CRERF)_pR⁴³,

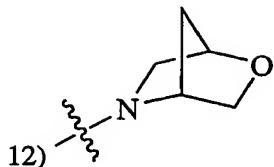
or R² and R⁸ are independently as defined above, and R⁹ and R¹⁰, together with the atoms to which they are attached, form the ring



R¹ is independently selected from:

20 1) hydrogen,
2) halogen,
3) CN,
4) OR⁴⁰,
5) N(R⁴⁰R⁴¹),
6) C(O)OR⁴⁰,
7) R⁸¹,
25 8) S(O)O-2R⁶,
9) N(R⁴⁰)(CR^aR^b)_nR⁶, wherein R⁶ = R⁸³,
10) N(R⁴⁰)(CR^aR^b)_nN(R⁴¹R⁴²),



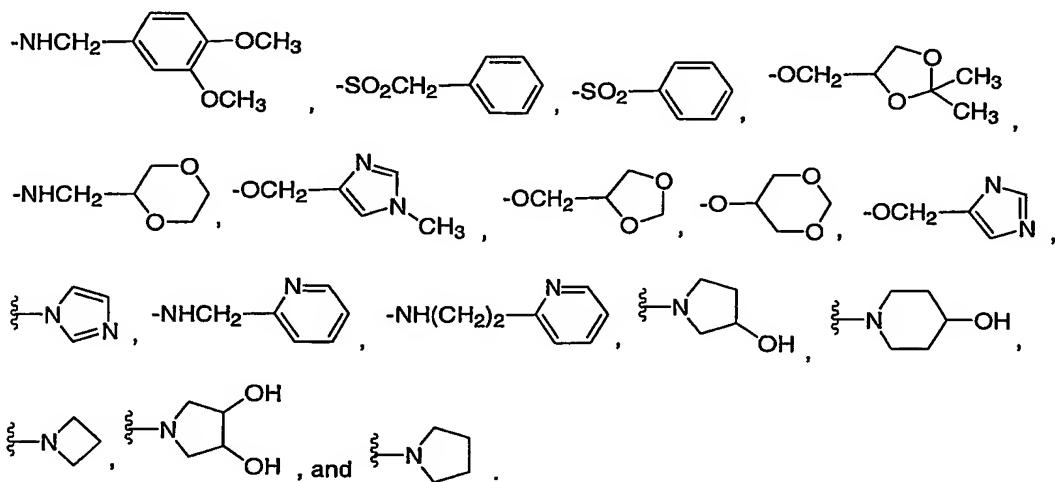
13) $\text{C}(\text{O})\text{N}(\text{R}^{41}\text{R}^{42})$, and

14) a 4-, 5-, or 6-membered heterocyclic ring containing 1 nitrogen atom, unsubstituted, or mono-, di- or tri-substituted with -OH.

5

3. A compound of Claim 2, or a pharmaceutically acceptable salt thereof, wherein R^2 , R^8 , and R^{10} are independently selected from hydrogen and halogen, and R^9 is OCH_3 or OCHF_2 .

4. A compound of Claim 3, or a pharmaceutically acceptable salt thereof, wherein R^1 is selected from the group consisting of hydrogen, $-\text{SCH}_3$, $-\text{SO}_2\text{CH}_3$, $-\text{NH}(\text{CH}_2)_3\text{OH}$, $-\text{NH}(\text{CH}_2)_2\text{OH}$, $-\text{NH}(\text{CH}_2)_2\text{OCH}_3$, $-\text{NH}(\text{CH}_2)_3\text{OCH}_3$, $-\text{NH}(\text{CH}_2)_2\text{NH}_2$, $-\text{NH}_2$, $-\text{SO}_2\text{CH}_2\text{CH}_3$, $-\text{CN}$, Cl , $-\text{OCH}_3$, $-\text{OCH}_2\text{CHCH}_2$, $-\text{OCH}_2\text{CH}(\text{OH})\text{CH}_2\text{OH}$, $-\text{NHCH}_2\text{CHCH}_2$, $-\text{CH}_3$, $-\text{CH}_2\text{CH}_2\text{OH}$, $-\text{O}(\text{CH}_2)_2\text{CHCH}_2$, $-\text{O}(\text{CH}_2)_2\text{CH}(\text{OH})(\text{CH}_2\text{OH})$, $-\text{NHCH}(\text{CH}_2\text{OH})_2$, $-\text{NHCH}_2\text{CH}(\text{OH})\text{CH}_2\text{OH}$, $-\text{NH}(\text{CH}_2)_2\text{CH}(\text{OH})\text{CH}_2\text{OH}$,



5. A compound of Claim 4, or a pharmaceutically acceptable salt thereof, wherein A is selected from the group consisting of

20 1) phenyl, wherein any stable ring atom is unsubstituted or substituted with halogen,
2) pyridinyl, wherein any stable C ring atom is unsubstituted or substituted with halogen,

3) indolyl, wherein any stable C or N ring atom is unsubstituted or substituted with halogen, and
4) a heterocyclic ring selected from the group consisting of pyrrolidine, piperidine, piperazine, and azetidine, unsubstituted, mono-substituted or di-substituted with C₁-C₆ alkyl.

5 6. A compound of Claim 5, or a pharmaceutically acceptable salt thereof, wherein R⁵ is selected from the group consisting of CN and C₁-C₆ alkyl, wherein said alkyl is unsubstituted, mono-substituted with R²², di-substituted with R²² and R²³, tri-substituted with R²², R²³ and R²⁴, or tetra-substituted with R²², R²³, R²⁴ and R²⁵.

10 7. A compound of Claim 6, or a pharmaceutically acceptable salt thereof, selected from the group consisting of
[(6-methoxy-4-phenylisoquinolin-3-yl)methyl]dimethylamine,
1-(1-chloro-6-methoxy-4-phenylisoquinolin-3-yl)-N,N-dimethylmethanamine,
{[6-methoxy-1-(methylthio)-4-phenylisoquinolin-3-yl]methyl}dimethylamine,
15 [6-methoxy-1-(methylsulfonyl)-4-phenylisoquinolin-3-yl]methyl(dimethyl)amine oxide,
1-[6-methoxy-1-(methylsulfonyl)-4-phenylisoquinolin-3-yl]-N,N-dimethylmethanamine,
3-[(dimethylamino)methyl]-6-methoxy-4-phenylisoquinoline-1-carbonitrile,
2,3-Dimethyl-6-methoxy-4-phenylisoquinolinium hydroxide,
20 6-methoxy-1-(2-methoxyethoxy)-3-methyl-4-phenylisoquinoline,
{3-[(6-methoxy-3-methyl-4-phenylisoquinolin-1-yl)oxy]propyl}amine,
2-[(6-methoxy-3-methyl-4-phenylisoquinolin-1-yl)amino]ethanol,
6-methoxy-3-methyl-1-(methylsulfonyl)-4-phenylisoquinoline,
6-methoxy-N-(2-methoxyethyl)-3-methyl-4-phenylisoquinolin-1-amine,
N-(6-methoxy-3-methyl-4-phenylisoquinolin-1-yl)ethane-1,2-diamine,
25 6-methoxy-3-methyl-4-phenylisoquinoline,
N-(3,4-dimethoxybenzyl)-6-methoxy-3-methyl-4-phenylisoquinolin-1-amine,
6-methoxy-3-methyl-4-phenylisoquinolin-1-amine,
1-(ethylsulfonyl)-6-methoxy-3-methyl-4-phenylisoquinoline,
1-(ethylsulfonyl)-6-methoxy-3-methyl-4-phenylisoquinoline,

1-(benzylsulfonyl)-6-methoxy-3-methyl-4-phenylisoquinoline,
6-methoxy-3-methyl-4-phenyl-1-(phenylsulfonyl)isoquinoline,
6-methoxy-3-methyl-4-phenylisoquinoline-1-carbonitrile,
3-tert-butyl-6-methoxy-1-(2-methoxyethoxy)-4-phenylisoquinoline,
5 1-chloro-6-methoxy-4-phenylisoquinoline-3-carbonitrile,
6-methoxy-4-phenylisoquinoline-1,3-dicarbonitrile,
1-(allyloxy)-6-methoxy-4-phenylisoquinoline-3-carbonitrile,
1-(2,3-dihydroxypropoxy)-6-methoxy-4-phenylisoquinoline-3-carbonitrile,
(allylamino)-6-methoxy-4-phenylisoquinoline-3-carbonitrile,
10 (+/-)-1-[(2,3-dihydroxypropyl)amino]-6-methoxy-4-phenylisoquinoline-3-carbonitrile,
1-[(2S)-2,3-dihydroxypropyl]amino}-6-methoxy-4-phenylisoquinoline-3-carbonitrile,
1-[(2R)-2,3-dihydroxypropyl]amino}-6-methoxy-4-phenylisoquinoline-3-carbonitrile,
(+/-)-1-[(2,2-dimethyl-1,3-dioxolan-4-yl)methoxy]-6-methoxy-4-phenylisoquinoline-3-
carbonitrile,
15 1-[(4S)-2,2-dimethyl-1,3-dioxolan-4-yl]methoxy}-6-methoxy-4-phenylisoquinoline-3-
carbonitrile,
1-[(4R)-2,2-dimethyl-1,3-dioxolan-4-yl]methoxy}-6-methoxy-4-phenylisoquinoline-3-
carbonitrile,
1-[(2R)-2,3-dihydroxypropyl]oxy}-6-methoxy-4-phenylisoquinoline-3-carbonitrile,
20 1-[(2S)-2,3-dihydroxypropyl]oxy}-6-methoxy-4-phenylisoquinoline-3-carbonitrile,
(+/-)-1-[(2,3-dihydroxypropyl)oxy]-6-methoxy-4-phenylisoquinoline-3-carbonitrile,
1-[(3R)-3-hydroxypyrrolidin-1-yl]-6-methoxy-4-phenylisoquinoline-3-carbonitrile,
1-[(3S)-3-hydroxypyrrolidin-1-yl]-6-methoxy-4-phenylisoquinoline-3-carbonitrile,
(+/-)-1-[3-hydroxypyrrolidin-1-yl]-6-methoxy-4-phenylisoquinoline-3-carbonitrile,
25 1-[cis-3,4-dihydroxypyrrolidin-1-yl]-6-methoxy-4-phenylisoquinoline-3-carbonitrile,

6-methoxy-4-phenyl-1-pyrrolidin-1-ylisoquinoline-3-carbonitrile,
6-methoxy-1-(methylsulfonyl)-4-phenylisoquinoline-3-carbonitrile,
6-methoxy-4-phenylisoquinoline-3-carbonitrile,
1,6-dimethoxy-4-phenylisoquinoline-3-carbonitrile,
5 1-chloro-4-(3-fluorophenyl)-6-methoxyisoquinoline-3-carbonitrile,
4-(3-fluorophenyl)-6-methoxyisoquinoline-3-carbonitrile,
4-(3-fluorophenyl)-6-methoxy-1-methylisoquinoline-3-carbonitrile,
4-(3-fluorophenyl)-1-[(2-hydroxyethyl)amino]-6-methoxyisoquinoline-3-carbonitrile,
10 1-amino-4-(3-fluorophenyl)-6-methoxyisoquinoline-3-carbonitrile,
4-(3-fluorophenyl)-1-[(3-hydroxypropyl)amino]-6-methoxyisoquinoline-3-carbonitrile,
1-(but-3-enyloxy)-4-(3-fluorophenyl)-6-methoxyisoquinoline-3-carbonitrile,
(+/-)-1-(2,3-dihydroxypropoxy)-4-(3-fluorophenyl)-6-methoxyisoquinoline-3-carbonitrile,
1-[(2R)-2,3-dihydroxypropoxy]-4-(3-fluorophenyl)-6-methoxyisoquinoline-3-carbonitrile,
1-[(2S)-2,3-dihydroxypropoxy]-4-(3-fluorophenyl)-6-methoxyisoquinoline-3-carbonitrile,
15 (+/-)-1-(3,4-dihydroxybutoxy)-4-(3-fluorophenyl)-6-methoxyisoquinoline-3-carbonitrile,
(+/-)-1-[(3R)-3,4-dihydroxybutoxy]-4-(3-fluorophenyl)-6-methoxyisoquinoline-3-carbonitrile,
1-[(3S)-3,4-dihydroxybutoxy]-4-(3-fluorophenyl)-6-methoxyisoquinoline-3-carbonitrile,
(+/-)-1-[(1,4-dioxan-2-ylmethyl)amino]-4-(3-fluorophenyl)-6-methoxyisoquinoline-3-
carbonitrile,
20 1-[(1,4-dioxan-(2R)-2-ylmethyl)amino]-4-(3-fluorophenyl)-6-methoxyisoquinoline-3-
carbonitrile,
1-[(1,4-dioxan-(2S)-2-ylmethyl)amino]-4-(3-fluorophenyl)-6-methoxyisoquinoline-3-
carbonitrile,
4-(3-fluorophenyl)-6-methoxy-1-[(1-methyl-1H-imidazol-4-yl)methoxy]isoquinoline-3-
25 carbonitrile,

(+/-)-1-(1,3-dioxolan-4-ylmethoxy)-4-(3-fluorophenyl)-6-methoxyisoquinoline-3-carbonitrile,

1-(1,3-dioxolan-(4R)-4-ylmethoxy)-4-(3-fluorophenyl)-6-methoxyisoquinoline-3-carbonitrile,

1-(1,3-dioxolan-(4S)-4-ylmethoxy)-4-(3-fluorophenyl)-6-methoxyisoquinoline-3-carbonitrile,

5 1-(1,3-dioxan-5-yloxy)-4-(3-fluorophenyl)-6-methoxyisoquinoline-3-carbonitrile,

4-(3-fluorophenyl)-1-{{2-hydroxy-1-(hydroxymethyl)ethyl}amino}-6-methoxyisoquinoline-3-carbonitrile,

10 4-(3-fluorophenyl)-1-(1H-imidazol-5-ylmethoxy)-6-methoxyisoquinoline-3-carbonitrile,

1-{{(2R)-2,3-dihydroxypropyl}amino}-4-(3-fluorophenyl)-6-methoxyisoquinoline-3-carbonitrile,

1-{{(2S)-2,3-dihydroxypropyl}amino}-4-(3-fluorophenyl)-6-methoxyisoquinoline-3-carbonitrile,

(+/-)-1-{{(2,3-dihydroxypropyl}amino}-4-(3-fluorophenyl)-6-methoxyisoquinoline-3-carbonitrile,

15 1-(1H-imidazol-1-yl)-6-methoxy-4-phenylisoquinoline-3-carbonitrile,

6-methoxy-4-phenyl-1-[(pyridin-2-ylmethyl)amino]isoquinoline-3-carbonitrile,

6-methoxy-4-phenyl-1-[(2-pyridin-2-ylethyl)amino]isoquinoline-3-carbonitrile,

(+/-)-1-[(3,4-dihydroxybutyl)amino]-4-(3-fluorophenyl)-6-methoxyisoquinoline-3-carbonitrile,

20 1-[(3R)-(3,4-dihydroxybutyl)amino]-4-(3-fluorophenyl)-6-methoxyisoquinoline-3-carbonitrile,

1-[(3S)-(3,4-dihydroxybutyl)amino]-4-(3-fluorophenyl)-6-methoxyisoquinoline-3-carbonitrile,

1-chloro-4-(2-fluorophenyl)-6-methoxyisoquinoline-3-carbonitrile,

25 4-(2-fluorophenyl)-6-methoxyisoquinoline-3-carbonitrile,

(+/-)-1-[(2,3-dihydroxypropyl)amino]-4-(2-fluorophenyl)-6-methoxyisoquinoline-3-carbonitrile,

1-[(2S)-(2,3-dihydroxypropyl)amino]-4-(2-fluorophenyl)-6-methoxyisoquinoline-3-carbonitrile,

5 1-[(2R)-(2,3-dihydroxypropyl)amino]-4-(2-fluorophenyl)-6-methoxyisoquinoline-3-carbonitrile,

(+/-)-6-(difluoromethoxy)-1-{[2,3-dihydroxypropyl]amino}-4-(3-fluorophenyl)isoquinoline-3-carbonitrile,

10 6-(difluoromethoxy)-1-{[(2S)-2,3-dihydroxypropyl]amino}-4-(3-fluorophenyl)isoquinoline-3-carbonitrile,

6-(difluoromethoxy)-1-{[(2R)-2,3-dihydroxypropyl]amino}-4-(3-fluorophenyl)isoquinoline-3-carbonitrile,

(+/-)-6-(difluoromethoxy)-1-{[2,3-dihydroxypropyl]oxy}-4-(3-fluorophenyl)isoquinoline-3-carbonitrile,

15 6-(difluoromethoxy)-1-{[(2S)-2,3-dihydroxypropyl]oxy}-4-(3-fluorophenyl)isoquinoline-3-carbonitrile,

6-(difluoromethoxy)-1-{[(2R)-2,3-dihydroxypropyl]oxy}-4-(3-fluorophenyl)isoquinoline-3-carbonitrile,

1-(4-hydroxypiperidin-1-yl)-6-methoxy-4-phenylisoquinoline-3-carbonitrile,

20 1-azetidin-1-yl-6-methoxy-4-phenylisoquinoline-3-carbonitrile,

(+/-)-1-[trans-3,4-dihydroxypyrrolidin-1-yl]-6-methoxy-4-phenylisoquinoline-3-carbonitrile,

1-[(3R,4R)-3,4-dihydroxypyrrolidin-1-yl]-6-methoxy-4-phenylisoquinoline-3-carbonitrile,

1-[(3S,4S)-3,4-dihydroxypyrrolidin-1-yl]-6-methoxy-4-phenylisoquinoline-3-carbonitrile, and

6-methoxy-N-(3-methoxypropyl)-3-methyl-4-phenylisoquinolin-1-amine.

8. A method of treating a condition in a mammal, the treatment of which is effected or facilitated by Kv1.5 inhibition, which comprises administering a compound of Claim 1 in an amount that is effective at inhibiting Kv1.5.

5 9. A method of Claim 8, wherein the condition is cardiac arrhythmia.

10 10. A method of Claim 9, wherein the cardiac arrhythmia is atrial fibrillation.

11. A method of Claim 9, wherein the cardiac arrhythmia is selected from the group
10 consisting of atrial flutter, atrial arrhythmia and supraventricular tachycardia.

12. A method of preventing a condition in a mammal, the prevention of which is effected or facilitated by Kv1.5 inhibition, which comprises administering a compound of Claim 1 in an amount that is effective at inhibiting Kv1.5.

15 13. A method of Claim 12, wherein the condition is cardiac arrhythmia.

14. A method of Claim 13, wherein the cardiac arrhythmia is atrial fibrillation.

20 15. A method of Claim 13, wherein the cardiac arrhythmia is selected from the group
consisting of atrial flutter, atrial arrhythmia and supraventricular tachycardia.

16. A method of Claim 12, wherein the condition is a thromboembolic event.

25 17. A method of Claim 16, wherein the thromboembolic event is a stroke.

18. A method of Claim 12, wherein the condition is congestive heart failure.

30 19. A pharmaceutical formulation comprising a pharmaceutically acceptable
carrier and the compound Claim 1 or a pharmaceutically acceptable crystal form or hydrate thereof.

20. A pharmaceutical composition made by combining the compound of Claim 1
and a pharmaceutically acceptable carrier.

21. A method of treating cardiac arrhythmia comprising administering a compound of Claim 1 with a compound selected from one of the classes of compounds consisting of antiarrhythmic agents having Kv1.5 blocking activities, ACE inhibitors, angiotensin II antagonists, cardiac glycosides, L-type calcium channel blockers, T-type calcium channel blockers, selective and nonselective beta blockers, endothelin antagonists, thrombin inhibitors, aspirin, nonselective NSAIDs, warfarin, factor Xa inhibitors, low molecular weight heparin, unfractionated heparin, clopidogrel, ticlopidine, IIb/IIIa receptor antagonists, 5HT receptor antagonists, integrin receptor antagonists, thromboxane receptor antagonists, TAFI inhibitors and P2T receptor antagonists.

5

10 22. A method for inducing a condition of normal sinus rhythm in a patient having atrial fibrillation, which comprises treating the patient with a compound of Claim 1.

23. A method for treating tachycardia in a patient which comprises treating the patient with an antitachycardia device in combination with a compound of Claim 1.